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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/555,102 07/17/00 THOMAS

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EXAMINER

GABEL, G

ART UNIT

PAPER NUMBER

1641

DATE MAILED:

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09/26/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/555,102

Applicant(s)

THOMAS, NICHOLAS

Examiner

Gailene R. Gabel

Art Unit

1641

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 July 2000.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-11 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-11 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Claims Under Examination

1. Claims 1-11 drawn to multiple assay method and kit therefore are under examination.

Specification

2. The following contents of the specification lack a title identifying them
 - (A) Background of the Invention:
 - (B) Brief Summary of the Invention:
 - (C) Brief Description of the Several Views of the Drawing(s):
 - (D) Detailed Description of the Invention:
 - (E) Claim or Claim:

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, step b) lacks clear antecedent support in reciting "the N population of labeled carrier beads" because the "carrier beads" recited in step a) does not appear to recite a label for the carrier beads.

Claim 1 step b) is ambiguous in reciting "dispensing each of the N populations of carrier beads into one of N different reaction vessels" because as recited, it appears that all the populations of carrier beads are being dispensed onto only one reaction vessel out of the N different reactions vessels which is probably not Applicant's intent.

Claim 1 step c) is ambiguous in reciting "dispensing each of the N samples into one of the said different reaction vessels" because as recited, it appears that all the N samples are being dispensed onto only one reaction vessel out of the N different reactions vessels which is probably not Applicant's intent.

Claim 1, step d) is vague and indefinite in reciting, "providing ... reagents for performing assay" because Applicant implies but does not distinctly recite how the inclusion of the reagent for use in the assay is effected. For example, are the reagents "coated into the reaction vessels" or coated into the carrier beads" or "dispensed into the reaction vessels." See also claim 10.

Claim 1, step d) is ambiguous in reciting "a signal moiety is caused to be partitioned in a compound-related manner between the carrier beads in that reaction vessel and a supernatant fluid" because it is unclear what is encompassed by the phrase "partitioned in a compound-related manner"; specifically, the term "compound-related" is a subjective effect that lacks a comparative basis for defining its metes and

bounds. Lastly, it is unclear what structural or functional cooperative relationship exists between the "reagents" and the "supernatant fluid" in the claim. Please clarify.

Claim 1, step d) lacks clear antecedent support in reciting "that reaction vessel".

Claim 1, step e) is vague in relation to previous steps b) - c) or b) - d) in reciting, "combining the contents of all the reaction vessels" because steps b) and c) appear to have only recited dispensing elements into "one of N different reaction vessels."

Claim 1, step f) is indefinite in reciting, "the signal moiety associated with each of a sequence of individual beads" because it is unclear what is encompassed by the term "associated" as used in the claim.

Claim 2-11 have improper antecedent basis problems in reciting, "A method as claimed in claim"

Claim 4 is indefinite in reciting, "the label associated with each of a sequence of individual beads" because it is unclear what is encompassed by the term "associated" as used in the claim. Further, it is unclear how the "populations of beads" relate structurally and functionally to the "sequence of individual beads"

Claim 4 lacks antecedent support in reciting, "the biological activity".

Claim 6 is indefinite in reciting, "the beads are pre-coated with a reagent" because it is unclear how the reagent in this claim relates to the reagents set forth in claim 1 which are "provided".

Claim 7 has improper antecedent basis problem in reciting, "a population of beads".

Claim 8 has improper antecedent basis problem in reciting, "a population of beads".

Claim 9 is ambiguous in reciting, "the signal moiety is a fluorescent dye" because it does not distinctly define how this fluorescent dye differs from the fluorescent dye that is effected in the previous claims, i.e. claim 4 and claim 7 so as to provide a differential distinction between the two elements recited.

Claim 11 lacks proper antecedent support in reciting, "the same reagent" and "the same surface concentration". Further, it is unclear how the recitation of "a supply of reagents" in this claim relates to the other reagent, i.e. "same reagent" in the previous occurrence in this claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

4. Claims 1-7 and 9-10 are rejected under 35 U.S.C. 102(e) as being anticipated by Yamashita et al. (US 6,210,900).

Yamashita et al. disclose a method for identifying test compounds having desired characteristics and identifying essential moieties in a lead structure which comprises preparing one or more encoded combinatorial libraries from a specified set of reaction

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sequences wherein the test compounds are tested for biological activity (pharmaceutical activity). Specifically, Yamashita et al. disclose providing populations of labeled (tagged) beads with fluorescently labeled identifiers attached thereto for encoding the combinatorial libraries (see Summary). Each population of beads are distinguishable from other populations by virtue of size, composition, fluorescent marker, and fluorescent label identifier. The identifier is a "coding" label attached to a population of beads by adding ratios of a fluorophore and a non-fluorophore or adding multiple different fluorophores in varying ratios (see column 3, lines 38-55). Yamashita et al. disclose that the number of readily distinguishable populations of beads correspond to the number of alternative variables in a registry. Yamashita et al. disclose dispensing an entirety of a population in a separate reaction vessel or well of a microtiter plate; beads usually are divided into populations of 1000 or more (see column 4, lines 16-37). Thereafter, appropriate reagents are added to each individual reaction vessel for reaction or assay to take place. After washing, the populations of beads are combined into a single mixture and subjected to flow cytometry for sorting (see column 4, lines 38-49). The compounds of the library can be tested using samples in a soluble receptor assay (see column 13, lines 1-7).

5. Claims 1-2, 4, 6-7, and 9-10 are rejected under 35 U.S.C. 102(e) as being anticipated by Chandler et al. (US 5,981,180).

Chandler et al. disclose multiplexed analysis of samples each containing test compounds (analytes) (see column 7, lines 25-61). Chandler et al. disclose providing

populations of carrier beads (beadsets or bead subsets) labeled with an appropriate reactant such as a biomolecule or a DNA sequence (see column 7, line 63 to column 6, line 9). Each population of beads is homogeneous and differing in at least one distinguishable parameter from other populations. Distinguishable parameters include size, shape, labels which have fluorescent emissions in more than one wavelength resulting from the presence of two or fluorochromes on the beads, etc. The classification parameter for each population is known and therefore the identity of each population can be verified using flow cytometry (see column 3, line 65 to column 4). Each bead population is coated with different reactants so as to bind or react and detect different compounds. For more quantitative analysis of compounds and biological activity (kinetic studies), each population of beads may be coated with a same reactant but at different concentrations so as to produce populations varying in density of precoated reactant rather than type of reactant; thereby allowing a parameter to serve as an indicator of reactant identity or reactant density.

6. Claims 1-10 are rejected under 35 U.S.C. 102(e) as being anticipated by Dower et al. (US 6,165,717).

Dower et al. synthesize nonporous solid supports which are carrier beads (particles) comprising a single bead or a populations of beads (two or more linked particles) for use in methods of identifying multiple compounds in samples. Each population of beads has coated, thereto, identifier tags which may have any recognizable features that carry required information that is distinguishable between

each population (see column 2, line 64 to column 3, line 21). The identifier tag in each population may be an oligonucleotide preferably composed of pyrimidines or it may be any recognizable feature that is microscopically distinguishable in size, shape, color, optical density; chemically reactive; magnetically or electronically encoded, etc. (see column 4, lines 26-38 and column 8, lines 35-50). The populations of beads are also coated with ligands that have affinity for specific compounds. Compounds or receptors which can be investigated using the carrier beads in an assay include drugs. To synthesize oligomers, the populations of beads are apportioned in a stochastic manner among a plurality of reaction vessels, pooled, and then further apportioned and pooled again in a series of twenty times then subjecting them to flow cytometry (see columns 9-10).

7. Claims 1-2, 4, 6-7, and 9-10 are rejected under 35 U.S.C. 102(e) as being anticipated by Haugland et al. (US 5,723,218)

Haugland et al. disclose fluorescent labeled carrier beads for use in flow cytometric detection of the presence of at least one test compound (analyte). The carrier beads are precoated with reactants (bioreactive substances) that react with or bind to compounds (biomolecules, hormones, vitamins, (see column 13, lines 33-67). Haugland et al. inherently disclose fluorescently-labeled carrier beads as populations or subsets of beads exhibiting one or more specific distinguishable parameters between each population because in the developing fluorescent beads, Haugland identified physical, biological, chemical, magnetic, and spectral properties as properties that can

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distinguish one particle or populations of particle from another, either singly or multiply, such as size or shape, type of reactant coated, hydrophobicity or hydrophilicity, gold plated or non-gold plated, and excitation and emission capacities as dictated by the type of fluorescence, respectively, to name a few. Haugland et al. teach that the beads labeled with dipyrrometheneboron difluoride can be developed using carefully optimized procedures so that large populations of uniformly labeled beads with specific differential and distinguishable parameters can be created with desired (physical) properties such as size and charge density such as taught in the instant invention (column 11, lines 21-49).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. Claims 8 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yamashita et al. (US 6,210,900) in view of Mandecki (US 5,641,634).

Yamashita et al. has been discussed supra. Yamashita et al. differ in failing to disclose that the beads populations are electronically labeled. Yamashita et al. also differ in failing to disclose a kit.

Mandecki et al. disclose a multiplex assay using electronically encoded carrier beads (solid phase particles associated with transponders) that are assigned a unique

index number which can be retrieved by a scanner device at any time during an assay for a compound. According to Mandecki et al., the carrier beads are analyzed to detect a label indicative of a reaction or binding of the compound to the carrier bead such as fluorescence, color, or radioactivity. Analysis is then preceded or followed by the decoding of the index number from the transponder. Both analysis and decoding can be done using two different instruments : a fluorimeter and a scanner. Mandecki et al. also disclose a kit for detecting biomolecular compounds in samples using carrier beads, assay vessels, coated labeled reagent (see columns 1-3).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to further electronically encode the populations of beads as disclosed by Mandecki so as to be an added "another" decipherable parameter in the bead populations in the method as taught by Yamashita because Mandecki specifically disclosed its applicability in multiplex assays. One of ordinary skill in the art at the time of the instant invention would have been motivated to incorporate the transponders of Mandecki into the method of Yamashita because Mandecki specifically disclosed their advantage in further detecting and differentiating increased number of analytes simultaneously in comparison to current multiplex assays.

Further, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to incorporate the reagents, labels and vessels taught by Yamashita into a kit arrangement such as in the disclosure of Mandecki because test kits are conventional and well known in the art for their recognized advantages of convenience and economy.

9. No claims are allowed.

Remarks

10. Prior art made of record are not relied upon but considered pertinent to the applicants' disclosure:

Lehnen et al. (US 5,567,627) disclose a method of detecting multiple subpopulations of analytes in samples employing reactants immobilized into labeled carrier beads.

Nolan et al. (US 6,287,766) disclose preparing an oligonucleotide primer bearing an immobilized capture tag, fluorescently labeled dideoxynucleotides, then binding the tagged primers to beads or microspheres, and measuring fluorescence by flow cytometry.

Watkins et al. (US 6,280,618) disclose a multiplex flow assay method using solid magnetic particles as the solid phase to facilitate separation of solid and liquid particles.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (703) 305-0807. The examiner can normally be reached on Monday-Thursday from 6:30 AM - 4:00 PM and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (703) 308-3399. The fax phone numbers for the

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organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gailene R. Gabel
September 21, 2001



LONG V. LE
SUPERVISORY PATENT EXAMINER
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09/24/01